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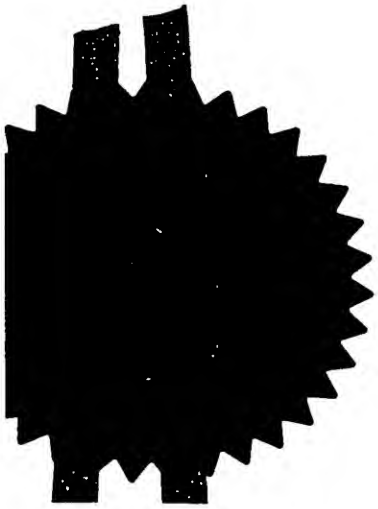

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Dated 10 August 2004

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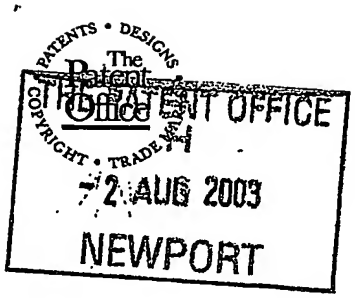

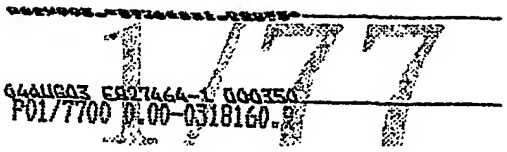

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1. Your reference

BQ/LAT/LW/P/24279.GB

2. Patent application number
(The Patent Office will fill in this part)

0318160.9

- 2 AUG 2003

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

SSL INTERNATIONAL plc
35 NEW BRIDGE STREET,
LONDON.
EC4V 6BW

Patents ADP number *(if you know it)*

7786874002

If the applicant is a corporate body, give the country/state of its incorporation

UNITED KINGDOM

4. Title of the invention

PARASITICIDAL COMPOSITION

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

WILSON GUNN M'CAW
41-51 ROYAL EXCHANGE
CROSS STREET
MANCHESTER
M2 7BD

Patents ADP number *(if you know it)*

7153927001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
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9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	11 ✓
Claim *(s)*	
Abstract	
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Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature Wilson Gunn M'Caw. Date 01/08/2003

12. Name and daytime telephone number of person to contact in the United Kingdom DR. LUCY TOVELL 0161-827-9400

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Parasiticidal Composition

The present invention relates to a parasiticidal composition which finds particular utility in the control of head lice infestation in humans.

Head lice infestation in humans is generally caused by insects from the families *Pediculidae* and *Pthiridas*, in particular *Pediculus humanus* species and *Pthirus pubis*.

The control of parasite infestation such as head lice has recently been managed by mosaic policies, with insecticides from the group consisting of dichlorodiphenyl trichloroethane (DDT), cyclodiens, organophosphates, carbamates and pyrethyroids as well as 'herbal' remedies such as tea-tree oil or other naturally derived terpenoid sources.

Head lice are known to become resistant to treatments, thus, to ensure availability of a diversity of insecticidal treatments there is a continuing requirement for novel insecticides to ensure suitable mosaic policies are maintained.

It is an object of the present invention to seek to provide alternative novel insecticides for the treatment of head lice.

According to the first aspect of the present invention there is provided a bioadhesive polymer for use in the treatment of head lice in humans.

According to the second aspect of the present invention there is provided the use of at least one bioadhesive polymer in the preparation of a composition for the treatment of head lice in humans.

According to a third aspect of the present invention there is provided a parasiticidal composition comprising at least one bioadhesive polymer and salts thereof as an active ingredient together with a physiological carrier.

Surprisingly, it has been found that bioadhesive polymers are highly effective in killing parasites and in particular those parasites responsible for head lice infestation. Thus, bioadhesive polymers have been found to have pediculicidal activity.

As referred to herein the term bioadhesive polymers, includes but is not limited to, carbomers, natural gums, thickeners, gelling agents and cellulose derivatives.

Preferably, the bioadhesive polymers of the present invention are carbomer related substances. Carbomers are high molecular weight network polymers consisting of acrylic acid backbones cross linked with polyalkenyl ethers. Typically carbomers have a molecular weight in the range of from 700 000 to 3-4 billion.

Where the bioadhesive polymer is a carbomer related substance the said substance shall preferably constitute at least about 0.05% by weight of the total composition.

The physiological acceptable carrier may be any suitable chemical entity that is compatible with human physiology and the bioadhesive polymer.

Examples of suitable physiological acceptable carriers, which may be used alone or in combination, include alcohols such as isopropanol, ethanol and industrial methylated spirit (IMS), water and/or silicone based compounds such as cyclomethicone

The composition of the present invention may further comprise at least one surfactant selected from any of the following: anionic, cationic, non-ionic, amphoteric or zwitterionic agents.

The anionic surfactants, which may be used alone or in combination, are preferably selected from the group comprising monovalent alkyl carboxylates, polyvalent alkyl carboxylates, acyl lactylates, alkyl ether carboxylates, N-acyl sarcosinates, N-acyl glutamates, fatty acid-polypeptide condensates, sulphuric acid esters, ester-linked sulphonates, alpha olefin sulphonates, phosphated ethoxylated alcohols.

The cationic surfactants, which may be used alone or in combination, are preferably selected from the group comprising monoalkyl and dialkyl quaternary ammonium compounds, amidoamines, aminimides and mixtures thereof.

The non-ionic surfactants, which may be used alone or in combination, are preferably selected from the group comprising polyoxyalcohols, polyoxypropylenes, amine oxides, fatty acid esters, polyhydric alcohols and mixtures thereof.

The amphoteric/zwitterionic surfactants, which may be used alone or in combination, are preferably selected from the group comprising triglycerides, e.g. lecithin, N-substituted alkyl amides, N-alkyl betaines, sulphobetaines, N-alkyl beta aminopropionates and mixtures thereof.

The aforementioned surfactants may also impart emulsifying properties to the composition of the present invention.

Preferably the pH of the composition of the present invention is in the range from 3 to 8.

The composition of the present invention may include additional ingredients, for example co-monomers such as $C_{10} - C_{30}$ alkyl acrylates. These alkyl acrylates are used to hydrophobically modify homopolymer carbomers to improve their electrolyte tolerance.

The composition of the present invention may further comprise a constituent having additional ovicidal activity. Such constituents result in the destruction of louse eggs even when the composition is in contact with hair for a relatively short period of time

Suitable ovicidal agents include a terpene, preferably one or both of d-limonene and geranyl acetate.

The composition of the present invention may be combined with at least one other pediculicidal and/or ovicidal agent such as d-phenothrin, malathion, carbaryl as well as natural ingredients such as tea tree oil and neem oil. Such agents may act synergistically with the composition of the present invention such that the efficacy of the composition is enhanced.

The composition of the present invention is thought to form a bioadhesive polymer network on the surface of the louse and egg. Thus, the composition is thought to be acting by suffocation and/or affecting water/electrolyte elimination in the louse/eggs i.e. osmoregulation.

According to the fourth aspect of the present invention there is provided a process for the preparation of a parasiticidal composition as hereinbefore defined comprising the step of bringing together at least one bioadhesive polymer and salts thereof and at least one physiologically acceptable carrier.

Preferably, the composition of the present invention is adapted for topical application to a subject.

Therefore, the composition of the present invention may be provided in any suitable form to allow such application, for example a gel, lotion, liquid, mousse (aerosol and non-aerosol), shampoo, crème rinse, serum, spray or emulsion for the hair.

The present invention will now be described further by way of example only with reference to the following experimental results.

Method of Testing the Pediculicidal/Ovicidal Activity of a Composition

Samples of Carbopol Ultrez 21 (manufactured by Noveon, Inc. and stated to be a hydrophobically modified cross-linked polyacrylate polymer) were used as an example of carbomers. Other carbomers may include but are not limited to Carbopol Ultrez 10, Carbopol ETD 2020 and 2050, Carbopol 980, 981, 971, 71G 1382, 2984, 5984, 934, 940, 941, 1342. Ultrez 21 was wetted with water, alcohol and surfactant were added into the Ultrez 21 water system and the formed gel was gently mixed. Finally, pH was adjusted to pH 5.7 to pH 6.9 with NaOH solution.

Measurement of the Activity by Immersion

Human lice, *Pediculus humanus*, were obtained from the culture colony maintained by Insect R&D Limited. Adult female and male lice, in approximately equal numbers, were used for each test. The lice were fed on the morning of the test and allowed a minimum of 4 hours to recover, during which time they were able to excrete excess water imbibed with their blood meal. Lice were counted into batches

that were provided with squares of open meshed nylon gauze (tulle), as a substrate upon which to stand, and each batch allocated to a marked 50-millimeter plastic Petri dish.

Louse eggs, *Pediculus humanus*, were obtained from the culture colony maintained by Insect R&D Limited. They were obtained by providing actively laying adult lice with a close meshed nylon substrate, in place of the normal cotton corduroy substrate, over a 48 hour period. At the end of this time the insects were removed and the gauze cut into appropriately sized smaller pieces. The small gauze pieces were randomly allocated to plastic Petri dishes in advance of the test.

For the test procedure the gauze bearing the lice/eggs was immersed in the fluid for 10 seconds, during which time the gauze was turned at least twice to ensure removal of air bubbles. After removal from the fluid the gauze and eggs were lightly blotted to remove any excess and returned the marked Petri dish.

Gauze squares bearing lice/eggs were incubated under normal maintenance conditions (30° ± 2° Celsius and 50% ± 15% relative humidity) for the remainder of the test period. At the end of the appropriate time the lice/eggs were washed for 30 seconds, using a 1:9 mixture of Boots frequent wash shampoo in tap water, and rinsed three times in warm (35° Celsius) tap water, poured over and through the gauze, followed by blotting with a medical wipe tissue. The gauze squares were then incubated under normal maintenance conditions until the results were recorded. Observations of the mortality of the lice were recorded after 24 hours and of louse eggs when the control group had completed emergence, a minimum of 10 days after treatment.

For these tests lice and eggs were exposed to the treatment overnight.

A control comparison test was performed using the 60% propan-2-ol (isopropanol), which is routinely used in our laboratory and causes minimum mortality to lice, in place of Carbopol gel. All other procedures for this comparator were the same as for the test groups.

Results

The formulations assessed against lice and eggs are summarised in Table 1.Table 1 Carbopol gel formulations.

Formulation	Composition [all% w/w]				
	Carbopol Ultrez 21	IPA	Softigen 767	Water	PH
1	0.5	-	-	to 100	5.89
2	0.5	1	5	to 100	5.8
3	0.5	1	5	To 100	6.82

The activity of the Carbopol gels on lice and eggs viability is shown in Tables 2.1 to 2.3., and Tables 3.1 to 3.2, respectively. Activity of these gels was effectively complete following overnight exposure with 0.5% w/w of Carbopol present. Dead lice showed signs of dehydration and most had burst guts so that they took on a dark red colour throughout the tissue.

Table 2.1 Pediculicidal efficacy of Carbopol formulation 1 following overnight exposure.

Formulation 1	Repl	Dead	Moribund	Alive	Mortality %	Corrected mortality
Active	1	20	0	0	100	100%
Control	1	4	0	16	20	-

Table 2.2 Pediculicidal efficacy of Carbopol formulation 2 following overnight exposure

Formulation 2	Repl	Dead	Moribund	Alive	Mortality %	Corrected mortality
Active	1	20	0	0	100	100%
	2	20	0	0	100	100%
	3	20	0	0	100	100%
Control	1	6	1	31	18.4	-

Table 2.3 Pediculicidal efficacy of Carbopol formulation 3 following overnight exposure

Formulation	Repl	Dead	Moribund	Alive	Mortality %	Corrected mortality
Active	1	21	0	0	100	100%
Control	1	4	0	16	20	-

Table 3.1 Ovicidal efficacy of Carbopol formulation 2 following overnight exposure (H-hatched, HH-half hatched, D-dead, UD-undeveloped)

Formulation 2	Repl	H	HH	D	UD	Mortality %	Corrected mortality
Active	1	0	0	9	215	100	100%
	2	0	0	7	247	100	100%
	3	0	0	19	481	100	100%
	4	0	0	0	167	100	100%
Control	1	170	1	13	42	24.8	-

Table 3.2 Ovicidal efficacy of Carbopol formulation 3 following overnight exposure (H-hatched, HH-half-hatched, D-dead, UD-undeveloped)

Formulation 3	Repl	H	HH	D	UD	Mortality %	Corrected mortality
Active	1	4	0	9	122	96.8	95.7%
Control	1	4	0	16		20	-

The description 'Moribund' includes any state in which the insect is deemed to be non-viable and unlikely to be able to continue life at the time of observation. Such insects may show only the slightest of movements of a limb or part of the gut but the

category extends through to walking insects that are considered sufficiently lacking in co-ordination that they would be unable to hold on their substrate, feed or lay eggs.

Mortality percentages were corrected by Abbott's formula (Abbott WS, Journal of Economic Entomology 1925; 1-8:265). Abbott's correction is a simple formula used to adjust observed test mortality figures to allow for any mortality in control groups:

$$CM = \frac{(T - C)}{(100 - C)} \times 100$$

Where:

CM	=	Corrected percent mortality
T	=	Percent mortality in the test group
C	=	Percent mortality in the control group

These results demonstrate that the Carbopol gel formulations are very effective pediculicidal and ovicidal agents.

Formulations

Formulations that can be prepared in aecordance with this invention include hair gels, lotions, liquids, mousses (aerosol and non-aerosol), shampoos, crème rinses, sprays or emulsion for the hair treatments. The precise nature and qualities of additional constituents that are required will vary according to the desired properties of the final product. The skilled formulator will be familiar with such constituents and their usage, which can include but it is not limited to, for example, silicone

compounds, suspending agents, emulsifying agents, surfactants, foaming agents and foam boosters, alcohol, emollients, preservatives, colourings and perfumes.

To enhance activity of the compositions according to the invention it has been found that further constituents having ovicidal activity can be added without adversely affecting their efficacy. These further constituents are terpenes and in particular, the terpenes d-limonene and geranyl acetate can be used, each at a concentration of from 0.2% v/v to 1% v/v.

It is of course to be understood that the invention is not intended to be restricted to the details of the above embodiments which are described by way of example only.